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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FOSTER, CHRISTINE E	

ART UNIT	PAPER NUMBER
1641	

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12/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/563,820	WINTHER ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 November 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: See *Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *88-90,92 and 95-104*.
   Claim(s) withdrawn from consideration: *91,93,94 and 105-116*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641

Continuation of 3. NOTE:

The proposed amendments raise new issues in that claim 88 now requires that the compact particle must have at least one dimension that is less than 1500 microns, a limitation that was not previously required by the claims. MPEP 714.13 states that Applicants cannot, as a matter of right, amend any finally rejected claims, except when an amendment merely cancels claims, adopts examiner suggestions, removes issues for appeal, or in some way requires only cursory review by the examiner. The newly introduced amendments to the claims were not presented earlier in prosecution and would require further search and consideration beyond cursory review by the examiner.

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant's arguments with respect to the rejections under 35 USC 102(b) are acknowledged (Reply, page 8) but are moot as they are directed to the new issues raised by the proposed amendments, which will not be entered for reasons discussed above.

With respect to the rejections of claims 88-90, 92, and 95-103 under 35 U.S.C. 103(a) as being unpatentable over Battifora et al. in view of Edge, Applicant's arguments have been fully considered but are not persuasive of error.

Applicant alleges impermissible hindsight (Reply, pages 9-10). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, it is maintained that motivation to combine the reference teachings is found in the references themselves, and in the general knowledge in the art at the time of the invention.

Applicant further argues that because Battifora focuses solely on reference standards that are genetically modified to express a detectable entity, and recognizes no shortcomings in their reference standards, Applicant concludes that as a result, the reference provides no motivation to modify the standards. This is not found persuasive because initially a teaching, suggestion, or motivation to combine the relevant prior art teachings does not have to be found explicitly in the prior art, as the teaching, suggestion, or motivation may be implicit from the prior art as a whole. In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336; cited with approval in KSR Int'l. Co. v. Teleflex Inc., 127 S. Ct. 1727, 82 USPQ2d 1385 (2007).

It is noted that the Battifora and Edge references employ the terminology "express" in a broader sense than Applicant, in essence to mean that the cell "bears" or "has" the antigen. This is made explicit in Edge since they use the term "express" to encompass chemically crosslinked antigens. Battifora also indicate that cells can be made to "express" antigen by means other than recombinant expression, as the reference also uses this term to refer to cell lines that possess defined amounts of endogenous antigens (Example 1; see column 4, lines 20-23). It is important to note here that because of this, the examiner disagrees with Applicant's characterization of Battifora as being focused solely on genetically modified reference standards (Reply, page 10). Rather, the reference standards that contain endogenous antigen produced through non-recombinant means.

In contrast, Applicants are apparently employing the term "express" in a narrower sense to refer only to those cells that produce detectable entity via expression of a gene for the detectable entity, either naturally or by recombinant gene expression (see especially [0232] and [0261] of the published application).

Battifora et al. teach cells that express a known amount of a target molecule as internal controls or standards immunohistochemistry. Although the reference does not contemplate chemical attachment of the target molecule, neither does the reference disparage or discourage this means of providing the cells with the known amount of target. Battifora et al. also contemplate other means of providing the cells with the target molecule other than via recombinant expression, such as by selection of cell lines that have defined amounts of antigen as discussed above.

Given the intended purpose of the internal control of Battifora, it is the examiner's judgment that one of ordinary skill in the art would understand that the relevant feature is that the cell must express (i.e., bear) a known amount of target, so as to allow for its use as a standard. See, e.g., column 2, lines 3-7: "[a]n important embodiment of the invention...thus provid[es] two or more cell lines expressing dissimilar known amounts of one antigen or known amounts of each of several antigens". As such, one of ordinary skill in the art at the time of the invention would take away from Battifora that the important thing is for the cell to have a known amount of antigen, and not that the cell must come to have the known amount of antigen by any one particular manner.

When taken together with the teachings of Edge that cells can be made to express antigens either by introducing genetic material encoding the antigens into cells (as in Battifora), or alternatively by chemically crosslinking antigens the surfaces of cells, it is maintained that it would have been obvious to one of ordinary skill in the art to produce the cells having known amounts of antigen of Battifora et al. by chemically crosslinking antigens to the surfaces of cells, rather than by introducing genetic material. One would be motivated to do this because the teachings of Edge establish that both methods were recognized in the art to be suitable for the same purpose, namely for producing cells that contain an antigen of interest in known amounts.

Applicant further argues that Edge and O'Leary do not describe any standardization system having features that could be combined with Battifora's system. See Reply, pages 10-11. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re

Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the Battifora reference has been relied upon for the teaching of the use of antigen-bearing cells as reference standards.

Applicant further argues that neither Edge nor O'Leary discusses any advantages from using reference standards having antigens that are chemically crosslinked. Applicant argues that they were the first to recognize the significant problems associated with reference standards that express detectable entities (as in Battifora) and to identify viable solutions. Applicant concludes that the prior art failed to recognize any reason to arrive at the claimed invention. See Reply, pages 10-11.

This is not found persuasive in the instant case, the art recognized equivalence of different means by which cells can be made to express antigens, as taught by Edge, provides motivation to combine the references. See MPEP 2144.06. Applicant does not clearly allege or document evidence of unexpected results in this regard. As such, it is maintained one of ordinary skill in the art would have been motivated to substitute chemical crosslinking (as taught by Edge) for genetic engineering (as exemplified by Battifora) in order to obtain cells that contain known amounts of antigen.

Applicant does not separately argue the limitations of dependent claim 104.

With respect to the provisional double patenting rejections, Applicant argues as above that Battifora and Edge do not teach or suggest a reference standard in which the compact particle does not express the detectable entity (Reply, pages 11-12), to which the examiner disagrees for the reasons set forth above.